# Development of The National Children's Study

*Pre-proposal conference*

March 7, 2007

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THE NATIONAL CHILDREN'S STUDY

# Study Rationale

- Converging factors
  - Increased vulnerability to environmental exposures among children
  - Exposures to some agents (lead, alcohol) have caused serious developmental effects
  - Known current exposures of high frequency—pesticides, phthalates, violence
  - Conditions with possible environmental cause – autism, birth defects, diabetes, learning disabilities

# Background and Rationale

President's Task Force on Environment and Health Risks to Children – appointed 1998, 2001, 2003

- Co-chairs Sec. HHS & Adm. EPA + 7 other cabinet member
- Charge: National strategies to control environ. risks
- Finds
  - Existing studies limited in size and scope
  - Longitudinal design to infer causality with multiple exposures and multiple outcomes
  - **Bold study** needed to identify effects or ensure safety

Children's Health Act of 2000:"..authorize NICHD to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children's health and development"

# Study Concepts

- Aims
  - Identify potential environmental effects: harmful, harmless, helpful
  - For important conditions and diseases of children, identify potential preventable causes
  - National resource for future studies
- Hypothesis driven
- Exposure begins with pregnancy
- Has power to study high priority conditions (n~100,000)
- Gene environment interaction
- National resource for future studies

# Planning Process for the NCS

- Interagency Coordinating Committee: NICHD, NIEHS, CDC, EPA
- Federally Chartered Advisory Committee
- Expert Working Groups
  - Hypotheses
  - Measures/methods

  Workshops (30)
- Literature reviews/white papers (20)
- Pilot Studies (25)
- Program Office Staff
- Study investigators (CC and Study Centers)

# Hypotheses necessary
## for framing the study

- Assure answers to “big issue” questions
- Hypothesis required for costly elements
- Important for child health & development
- Requires and measurable with sample ~100,000
- Evolving with the science
- Proving extremely valuable with protocol development
- Hypothesis statements on website -30

# Priority Health Outcomes/Exposures

| Priority Exposures | Examples |
|---|---|
| Physical Environment | Housing quality, neighborhood |
| Chemical Exposures | Pesticides, phthalates, heavy metals |
| Biologic Environment | Infectious agents, endotoxins, diet |
| Genetics | Interaction between genes and environment |
| Psychosocial milieu | Family structure, socio-economic status, parenting style, social networks, exposure to media and violence |

| Priority Health Outcomes | Examples |
|---|---|
| Pregnancy Outcomes | Preterm, Birth defects |
| Neurodevelopment & Behavior | Autism, learning disabilities, schizophrenia, conduct and behavior problems |
| Injury | Head trauma, Injuries requiring hospitalizations |
| Asthma | Asthma incidence and exacerbation |
| Obesity & Physical Development | Obesity,diabetes, altered puberty |

# Sampling and Center strategies

- National probability sample important
  - Exposure-outcome relationship representative of the U.S. population
  - Important exposures with varied and unknown distributions are not missed
  - Clustered for community attributes & logistics
- Centers of excellence important
  - Broad scientific input
  - Measures require center based expertise and facilities
- Probability sample by Centers
  - Unique combination
  - Requires flexibility and adaptation of center to the scientific design
  - Requires support and guidance by coordinating center

# National Children's Study Sample

**All Births in the Nation** → **~4 million births in 3,141 counties**

**Sample of Study Locations** → **105 Locations**

**Sample of Study Segments** → **Selection of neighborhoods**

**Study Households** → **All or a sample of households within neighborhoods**

**Study Women** → **All eligible women in the household**

# Study Sample by NCHS

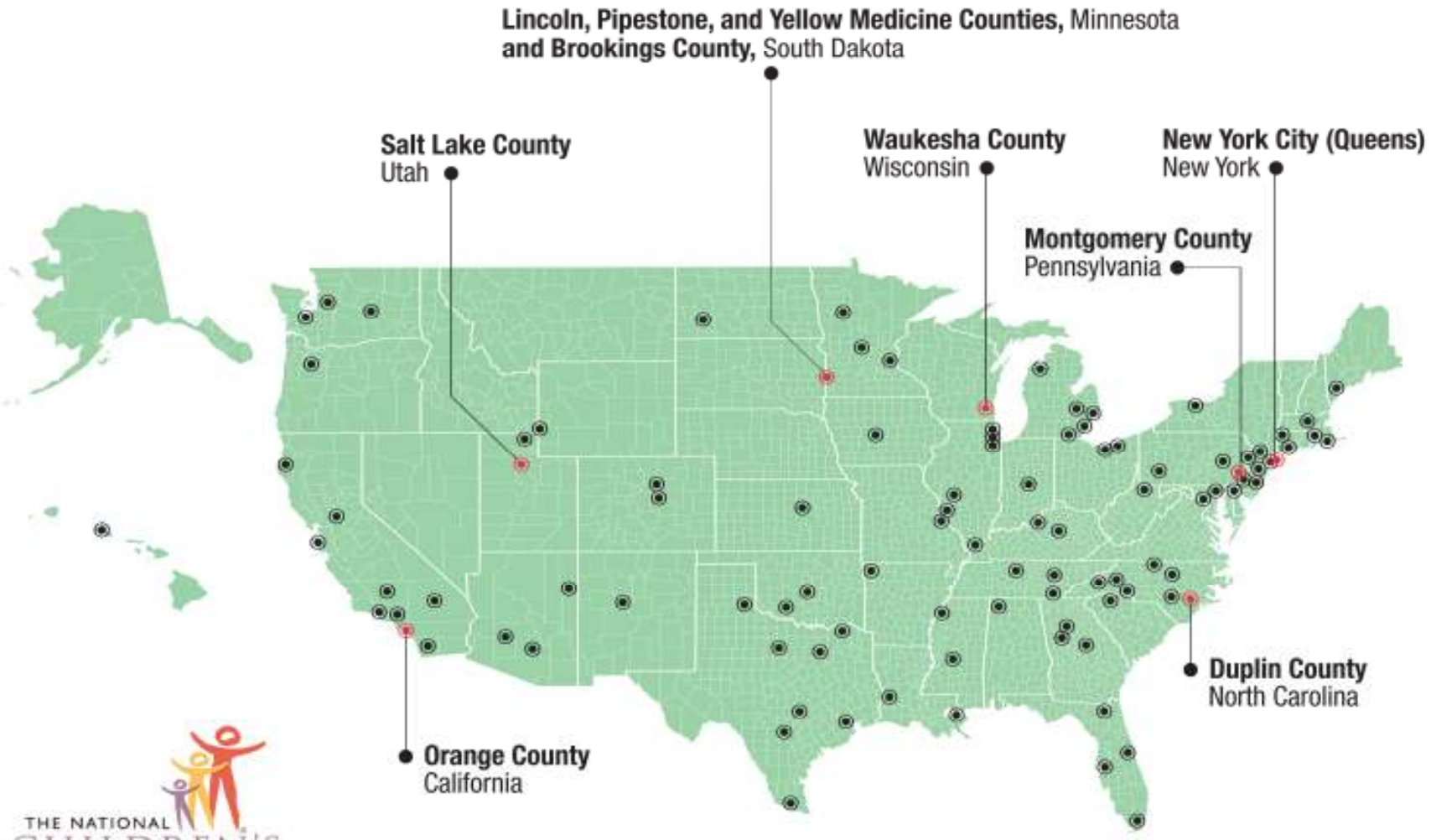
- National probability sample – known chance of inclusion
- 105 locations - roughly corresponding to counties, or clusters of adjoining counties; 79 metropolitan, 26 rural
- 13 self-representing counties;remaining counties placed into strata based on:
  - Metropolitan status
  - Geography
  - Average number of births per year
  - Race, ethnicity, percent low birth weight

# Locations vs. Centers

- Sites—geographic locations (counties) from which participants will be recruited
  - Selected by stratified probability sample of primary sampling units
  - 105 Locations
- Centers—entities or institutions that will carry out Study at the Locations
  - Selected by a competitive process
  - Each will cover more than one site
  - 30-50 Centers

# National Children's Study Locations

Vanguard locations: Study Centers awarded (bold)




February 2006

# Vanguard and Coordinating Centers established for the NCS

Coordinating Center:

WESTAT with Harvard Medical School, Univ. of Penn, and Daston Communications

Vanguard Centers:

Orange County, CA: University of CA—Irvine and Children's Hospital of Orange County

Queens, New York City: Mount Sinai School of Medicine, Columbia Mailman School of Public Health, U. Medicine and Dentistry of NJ and NYC Dept of Health and Mental Hygiene

Duplin County, NC: Univ. of North Carolina, Batelle Memorial Institute, and Duke University

Montgomery County, PA: Children's Hosp of Pennsylvania, Univ. of Pennsylvania, and Drexel University School of Public Health

Salt Lake County, Utah: University of Utah

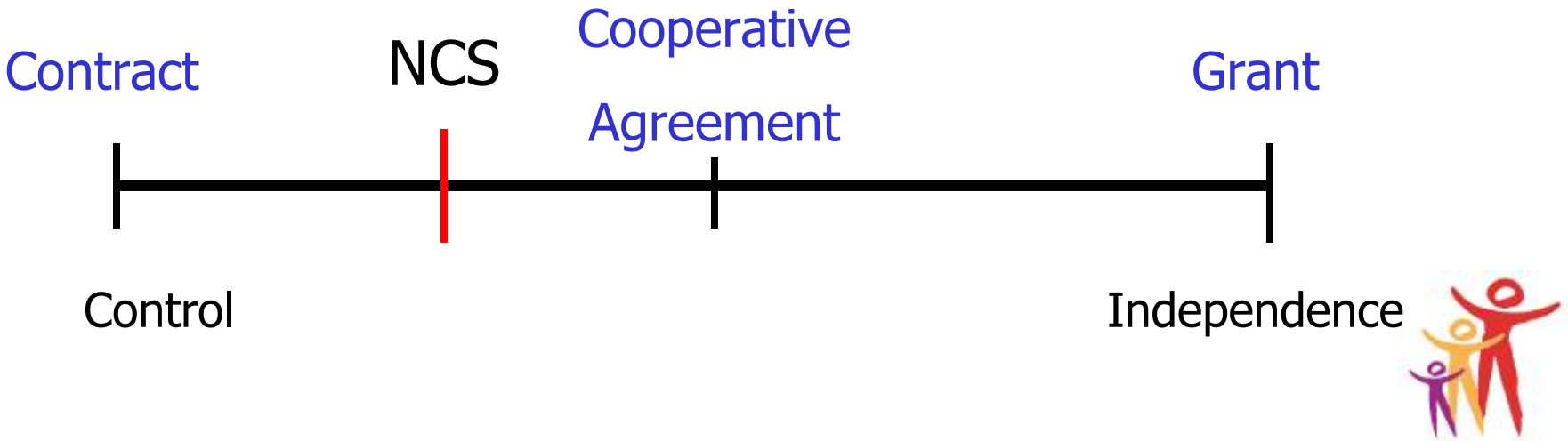
Waukesha County, WI: University of Wisconsin, Medical College of Wisconsin, NORC and a Consortium

Brookings, SD; Lincoln, Yellow Medicine, Pipestone MN: South Dakota State U., U. Cincinnati

# Why a contract mechanism?

To assure a consistent rigorous core protocol carried out at all sites

To assure NCS addresses goals of funding agencies



# Study Organization:
# Key Entities

Interagency Coordinating Committee (ICC) – Senior staff and scientists of supporting Federal Agencies: – Federal oversight

Federal Consortium – Representatives of Federal Agencies – Broad Federal input

National Children's Study Advisory Committee (NCSAC) – Review and advice

Program Office (PO) at NICHD – Day-to-day scientific and operational management

Steering Committee – Center PI's and Federal scientists – Primary scientific deliberations

Coordinating Center – Data management and clinical coordination

Data safety monitoring committee – monitor data and advise on interventions based on findings

# Steering Committee
## Roles and responsibilities

- Identifying problems and best practices that arise in the conduct of the study
- Scientific input/expertise to support decision-making
- Making recommendations regarding scientific content of a study component
- Review and approval (not the only) regarding adjunct/add-on studies
- Decision-making about non-direction changing (and budget neutral) issues related to the protocol and MOP
- Proposing changes to the protocol

# Study Components

- In place
  - Scientific support reviews, analyses, surveys
  - Information technology development Contractor (BAH, CC/Westat)
  - Clinical/data Coordinating Center (CC)
  - Initial/Vanguard Study Centers (7)
- Over this year
  - Wave I Study Locations (30+/-) and Study Centers (15-30)
- Following – 2007-08
  - Specimen Repository
  - Laboratory services (NCEH, EPA, contracts)

# Access to Data and Publication

- Maximum use and publication will be a guiding principle
- Primary hypotheses and analyses - Data access and analyses through Center PI's and other participating investigators (including Federal Agency Scientists) as per data access and publication policies (similar to other large multi-center studies)
- Data use and Publication Sub-committee of the Steering Committee drafting policies and providing oversight.
- Public use datasets to be available with each phase as per NIH guidelines, by confidentiality requirements.
- Federal statutes and contractual agreements will prevail.

# Adjunct studies

- Involve a portion of the sample using some NCS infrastructure and data to address additional or in-depth question
- Funding: R-01 or other grant, Public-private partnerships (foundation, industry, other), NCS
- Process for review and approvals established at NCS Program Office
- Examples
  - Genomic analysis of subgroup specimens for targeted gene-environment interactions
  - Functional neuro-imaging of exposed subgroup for mechanism of effect on child development
- Adjunct study proposals are **NOT** a requirement for this solicitation

# Projected Time Line

| | |
|---|---|
| 2000-present | Pilot studies/methods development |
| 2004 | Developed Study Design and Study Plan; Posted Requests For Proposals: Coordinating and Vanguard Centers |
| 2005 | Awarded initial contracts (Coordinating and Vanguard Centers) |
| 2005-2007 | Start-up phase for Vanguard Centers |
| 2007 | Completion of the first phase of the Study protocol |
| 2007 + | Requisite reviews and approvals (OMB, Peer review, IRB's) |
| 2007 | Post Requests for Proposals (RFP) for Wave I Study Centers |
| 2007 | Award Wave I Study Centers (contracts) |
| 2008-2012 | Enroll participants and begin the full Study at Vanguard Centers |
| 2007-2008 | Start-up phase for Wave I Study Centers |
| 2009-2012 | Enroll participants and begin full Study at additional centers |
| 2009 | First Study results become available (methods, pilots, preliminary) |
| 2013-2033 | Hypothesis-specific data analysis; publish data; public-use datasets |

# Funding (as of March 2007)

- FY 2000-06: ~ $50m from existing budgets of NICHD/EPA/CDC/NIEHS
  - Infrastructure: Study Plan; Coordinating Center and 7 Vanguard Study Centers…
  - Scientific development: 30 workshops, 20 scientific reviews, 19 pilot studies; hypotheses, exposure and outcome measures, protocol in progress…
- FY 2007: **$69m appropriated February 14**
  - Prepare for recruitment and enrollment at VG Centers
  - Develop Information Management System
  - Establish additional centers for expanded locations toward full sample
- FY 2008: No NCS funding in the President's FY 2008 budget, House Appropriations "intend to fund NCS"
- To conduct the full Study: FY 08-34
  - ~ $120m/year for 26 years

# Contact Information

Web site:
http://NationalChildrensStudy.gov

Listserv for news and communication

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